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No. 06-1249

IN THE

Supreme Court of the United States

WYETH,

Petitioner,

v.

DIANA LEVINE,

Respondent.

On Writ of Certiorari to the Supreme Court of Vermont

BRIEF OF JOHN E. CALFEE, ERNST R. BERNDT, ROBERT HAHN, TOMAS PHILIPSON, PAUL H. RUBIN, AND W. KIP VISCUSI AS *AMICI CURIAE* SUPPORTING PETITIONER

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INTEREST OF *AMICI CURIAE*[1]

Amici are economists and economics professors who teach and write on the economic impacts of regulation, including pharmaceutical regulation, and on health care policy, and who wish to ensure that

[1] The parties have consented to the filing of this *amicus* brief. Pursuant to Rule 37.6, *amici* state that this brief was not authored in whole or in part by counsel for any party, and that no person or entity other than *amici* or their counsel made a monetary contribution to the preparation or submission of this brief.

the Court fully considers the adverse effects that might arise from the Vermont Supreme Court's decision in *Wyeth v. Levine*, if that decision is upheld by the U.S. Supreme Court. *Amici* have no stake in the outcome of this case. They are filing this brief solely as individuals and not on behalf of the institutions with which they are affiliated.

John E. Calfee is a Resident Scholar at the American Enterprise Institute. He has written extensively on Food & Drug Administration (FDA) policy, health care policy, and the pharmaceutical and drug markets. Dr. Calfee is the author of many publications on pharmaceutical and health care issues. *See, e.g.,* John E. Calfee, *Price, Markets, and the Pharmaceutical Revolution* (2000) and Claude Barfield and John E. Calfee *Biotechnology and the Patent System: Balancing Innovation and Property Rights* (2007). Dr. Calfee previously was a visiting fellow at the Brookings Institution and an associate professor at the Boston University School of Management.

Ernst R. Berndt is the Louis B. Seley Professor of Applied Economics, Finance and Accounting at the MIT Sloan School of Management, Co-Director of the Biomedical Enterprise Program at Sloan School and the Harvard-MIT Division of Health Sciences and Technology, and Co-Director of the MIT Center for Biomedical Innovation. He has published widely in health economics and pharmaceutical regulation. Among his publications are *Opportunities for Improving the Drug Development Process: Results from a Survey of Industry and the FDA*, National Bureau of Economic Research working paper 11425 (with Adrian H. Gottschalk and Matthew W. Strobeck), and *Cost-benefit analysis of the FDA: The case of the*

prescription drug user fee acts, J. Pub. Econ. v. 92, No. 5-6, pp. 1306-1325 (June 2008) (with Tomas Philipson, Adrian H.B. Gottschalk, and Eric Sun).

Robert Hahn is executive director of the Reg-Markets Center and a senior fellow at the American Enterprise Institute. His research focuses on the costs and benefits of regulation. *See, e.g.,* Robert Hahn and Paul C. Tetlock, *Has Economic Analysis Improved Regulatory Decisions?*, J. Econ. Perspectives, Vol. 22, no. 1, pp. 67-84 (Winter 2008).

Tomas Philipson is a Professor at The Irving B. Harris Graduate School of Public Policy Studies and an associate member of the Department of Economics. He has been a visiting faculty member at Yale University, a visiting fellow at the World Bank, a Senior Economic Advisor to the head of the Food and Drug Administration (FDA), and Senior Economic Advisor to the head of the Centers for Medicare and Medicaid Services. Philipson has published widely on health economics and FDA regulation and twice received the Kenneth Arrow Award of the International Health Economics Association. *See, e.g., Cost-benefit Analysis of the FDA: The case of the prescription drug user fee acts*, J. Pub. Econ. v. 92, No. 5-6, pp. 1306-1325 (June 2008) (with Ernst R. Berndt, Adrian H.B. Gottschalk, and Eric Sun); and *Is the Food and Drug Administration Safe and Effective?*, J. Econ. Perspectives, vol. 22, no. 1, pp. 85-102 (Winter 2008) (with Eric Sun).

Paul H. Rubin is Samuel Candler Dobbs Professor of Economics and Law at Emory University and Editor in Chief of *Managerial and Decision Economics*. He has held several senior government positions, including Chief Economist at the U.S. Consumer Product Safety Commission and Assistant

Director in the Bureau of Economics at the Federal Trade Commission. He has published many articles on drug regulation and tort law and their effects. *See, e.g., Matching Prescription Drugs and Consumers: The Benefits of Direct Advertising*, 313 New Eng. J. Med. 513-515 (Aug. 22, 1985) (with Alison Masson).

W. Kip Viscusi is the University Distinguished Professor of Law, Economics, and Management at Vanderbilt University. He was previously a professor at Harvard Law School and the Duke University and Northwestern University departments of economics. He has written extensively on products liability, hazard warnings, and risk regulation generally. Among his publications are *Reforming Products Liability* (Cambridge: Harvard University Press, 1991); *Deterring Inefficient Pharmaceutical Litigation: An Economic Rationale for the FDA Regulatory Compliance Defense*, Seton Hall L. J., vol. 24, no. 3, pp. 1437-1480 (1994) (with Steven Rowland, Howard Dorfman, and Charles Walsh); and *Economics of Regulation and Antitrust*, 4th ed. (Cambridge; MIT Press, 2005) (with Joseph Harrington and John Vernon).

SUMMARY OF ARGUMENT

Prominent in arguments opposing preemption of state tort law liability for alleged inadequacies in prescription drug labeling is the argument that such liability can complement FDA regulation by improving on a regulatory scheme that fails to provide adequate deterrence against the marketing of unsafe or inadequately labeled drugs. The premise of this argument is faulty. Fundamental principles of economics and numerous studies of FDA drug regu-

lation reveal that FDA in fact errs on the side of overregulation of prescription drugs. Product liability litigation focused solely on one side of the prescription drug public health equation leads to further distortions of the drug approval and labeling process and exacerbates FDA's inherent overly cautious approach. Preemption of state tort law where it conflicts with FDA requirements will minimize these distortions and thereby maximize public health.

FDA's incentive to overregulate is clear upon examination of the underlying forces that can skew its regulatory decisionmaking. In particular, FDA faces substantial criticism when it mistakenly approves drugs that should not have been approved ("Type I errors"), but considerably less criticism when it fails to approve drugs that should have been approved ("Type II errors"). As a result, FDA has an incentive to be overly cautious in approving new drugs, even though the failure to approve a beneficial drug can lead to more significant public health harms than mistaken approval of potentially dangerous drugs. The same FDA tendency toward over-caution (Type II errors) carries over to regulation of the drug label, where FDA has an incentive toward over-warning and undue contraindications. Such excessive warning language also has adverse public health consequences.

State tort lawsuits exacerbate the problems of FDA's overly cautious approach by imposing additional requirements on pharmaceutical companies to add new warnings or contraindications. These requirements lead to a host of distortions in drug marketing and availability that have adverse consequences for public health and wellbeing. Preemption provides an important safeguard against

expected FDA Type II errors by countering the exacerbating impact of state tort lawsuits for failure to warn.

ARGUMENT

I. STATE TORT LAWSUITS EXACERBATE PROBLEMS CAUSED BY FOOD & DRUG ADMINISTRATION OVERREGULATION AND OVERWARNING

A. Incentives Facing FDA Regulators Result in Excess Caution in Drug Approval.

In approving the safety and efficacy, of prescription drugs, FDA faces the possibility of two types of error. First, it can approve a drug that should not have been approved because of safety problems. These errors are called Type I errors. Second, it can fail to approve a drug that should have been approved. These errors are called Type II errors. Under well-established economic principles, the question whether FDA is more likely to commit Type I errors or Type II errors can be answered by focusing on the societal or institutional incentives that push FDA to err on one side or the other.[2] Repeated economic investigation of this question indicates that FDA incentives are skewed toward excessive caution in the regulation of drug development and the approval of new drugs, *i.e.*, Type II errors.[3]

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[2] *See* Henry I. Miller, *First, Do No Harm*, Hoover Digest, No. 4 (2000), *available at* http://www.hoover.org/publications/digest/3493341.html.

[3] *See, e.g.*, Sam Peltzman, *Regulation of Pharmaceutical Innovation: The 1962 Amendments* (1974) ("These measurable effects [of missed benefits from slower new drug approvals, gains from reduced waste on ineffective drugs, and reduced

This skewing can be best understood by considering the likely consequences to FDA's image of a Type I versus a Type II error. When deciding whether the benefits of a proposed new drug exceed its risks, FDA staff know that if they commit a Type I error—the approval of a drug that turns out to be insufficiently safe once marketing begins—their error will become known. Because the harmful side-effects of the drug may be highly visible, a Type I error can and often does lead to impassioned criticism of the agency. On the other hand, a Type II error—the failure to permit marketing of a drug that would in fact provide benefits in excess of harms—is typically

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benefits from competition] add up to a net loss of $250 to $350 million, or about 6 percent of total sales"); Sam Peltzman, *An Evaluation of Consumer Protection Legislation: The 1962 Drug Amendments*, 81 J. Pol. Econ. 1049 (1973), *reprinted in Chicago Studies in Political Economy* 303-48 (George J. Stigler ed., University of Chicago Press 1988) (to same effect); William M. Wardell & Louis Lasagna, *Regulation and Drug Development* 97 (1975) ("In examining the balance sheet for individual therapeutic categories (Chapter VII), it was shown that, in many therapeutic areas, useful and even uniquely effective or safe drugs have been introduced in Britain substantially earlier than in the United States, and at any given time the United States lacks a number of such drugs."); Kenneth Kaitin & Jeffrey Brown, *A Drug Lag Update*, 29/2 Drug Info. J. 361, 372 (1995) (**"**Despite numerous regulatory reform efforts in this country directed toward accelerating drug development and review processes (described in detail in another section of this White Paper), the United States continues to lag behind other countries in the availability of important new therapeutic products."); Henry I. Miller, *To America's Health: A Proposal to Reform the Food and Drug Administration* 43 (2000) ("Type 2 errors in the form of unreasonable governmental requirements and decisions can delay the marketing of a new product, lessen competition to produce it, and inflate its ultimate price. They can even prevent marketing of a product entirely.").

known only by the relatively few persons who are intimately involved in developing the drug and are largely hidden from patients and the larger medical community who suffer the consequences of the error. Yet the adverse public health impact of a failure to approve a beneficial drug may be even more severe than the approval of an insufficiently safe drug.

Moreover, Type I errors in approving unreasonably unsafe drugs are often quickly corrected precisely because the public learns of the error. But the failure to approve a beneficial drug may go uncorrected for years, if at all. As a result, the net effect of the asymmetry in public knowledge and publicity is to bias even the best-intentioned FDA regulators towards excessive caution and delay in approving new drugs.

Recent debate over FDA's handling of drug safety, notably in connection with selective serotonin reuptake inhibitor (SSRI) antidepressants and Vioxx, an arthritis pain reliever, and culminating in a recent report from the Institute of Medicine, has made clear that the institutional incentives to avoid Type I errors at the expense of committing more Type II errors are very strong. Criticism of FDA staff in connection with the safety of recently approved drugs vastly exceeds any criticism of agency sluggishness in approving the hundreds of drugs in development in recent years. John E. Calfee, *The Vioxx Fallout*, *AEI Health Policy Outlook*, Sept.-Oct. 2005; Institute of Medicine, *The Future of Drug Safety: Promoting and Protecting the Health of the Public* (2006); John E. Calfee, *Playing Catch-up: The FDA, Science, and Drug Regulation*, *AEI Health Policy Outlook*, March 2006; Peter H. Schuck, *FDA Preemption of State Tort Law in Drug Regulation: Finding the Sweet*

Spot, Roger Williams U. L. Rev. (forthcoming 2008), *available at* http://ssrn.com/abstract=1078013 at 14-15.

Notably, however, there is no evidence that FDA's overly cautious approach has resulted in the approval of fewer unsafe drugs. To the contrary, numerous studies have concluded that FDA's many years of administrative delay in approving new drugs has caused reductions in the benefits to be gained from new drug development while contributing few, if any, tangible reductions in drug-related public health risks. For example, comparisons of drug approval regimes in the United States, Spain and the U.K. demonstrate that the more rapid drug approval timelines in the European countries have not led to an increased rate of subsequent drug safety withdrawals in those countries, as would be expected if FDA's cautious approach prevented the approval of unsafe drugs. Olav M. Bakke, et al., *Drug Safety Discontinuations in the United Kingdom, the United States, and Spain from 1974 through 1993: A Regulatory Perspective*, Clinical Pharmacology and Therapeutics vol. 58, p. 108 (1995) (noting post-approval drug withdrawals of, respectively, 3% in U.S. and Spain and 4% in U.K.). Likewise, various researchers—including the Institute of Medicine—have examined drug safety before and after the enactment in the United States of the Prescription Drug User Fee Act of 1992 and found that the procedures in the Act allowing faster new drug approvals have not resulted in any diminution of drug safety. *See* Institute of Medicine, *The Future of Drug Safety: Promoting and Protecting the Health of the Public* 3: 5-8 (2006) (reviewing the effects of the Prescription Drug User Fee Act of 1992). And a recent econometric study found that the faster drug

approval times secured under the Act have demonstrably improved consumer welfare. *See* Tomas Philipson et al., *Cost-benefit Analysis of the FDA: The case of the prescription drug user fee acts*, J. Pub. Econ. v. 92, No. 5-6, pp. 1306-1325 (June 2008); Tomas Philipson & Eric Sun, *Is the Food and Drug Administration Safe and Effective?*, J. Econ. Perspectives, vol. 22, no. 1, pp. 85-102 (Winter 2008).

B. The Same Perverse Incentives Result in Excess Caution by FDA in Drug Labeling.

When FDA approves a new drug, it also approves a detailed label to accompany the drug. The label contains indications (conditions to be treated), dosage, administration, and other details including warnings and contraindications, along with summaries of clinical trials and other data. These labels are designed for use by learned intermediary physicians (without whom prescription drugs may not be obtained), although others, including patients, may also make use of labels. As new information arrives about the risks and benefits of approved drugs, FDA continues to review the drug labels and effects labeling changes as appropriate. FDA employs specialized experts in the field to conduct this ongoing review and gathers voluminous post-marketing information from pharmaceutical firms, medical care providers, and other sources. *See*, *e.g.*, *Should FDA Drug and Medical Device Regulation Bar State Liability Claims?: Hearing Before the H. Comm. on Oversight & Gov't Reform* (testimony of Randall Lutter, FDA Deputy Commissioner for Policy) (May 14, 2008) ("Lutter Testimony").

FDA has long recognized that labels must give varying degrees of emphasis to specific items of information, and that labels should not contain all information of possible interest. *See* Final Rule, Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3968 (Jan. 24, 2006). FDA has for many years sought to modify and improve drug labels while avoiding the constant danger of overwarning. *Id.*; Lutter Testimony. If all potentially negative information were to be included, such as every known possible side-effect, two adverse consequences would follow. One is overwarning: the presence on labels of unfounded or disproportionately prominent warning information, which could deter or discourage drug use that would be beneficial after taking reasonable account of risks and benefits. The second is "clutter": the presence of so much information that physicians would find it hard to distinguish important information from relatively unimportant information and might not even bother to peruse all the information. 71 Fed. Reg. at 3935, 3968.

FDA's decisions about drug labels are strongly affected by the incentives faced by FDA staff. We have described how those incentives cause FDA to exercise excessive caution when approving new drugs. Similar reasoning applies to FDA decision-making about what risk and benefit information to require in drug labels. *See* W. Kip Viscusi, et al., *Deterring Inefficient Pharmaceutical Litigation: An Economic Rationale for the FDA Regulatory Compliance Defense*, Seton Hall L.J., vol. 24, pp. 1437, 1469 n.118 (1994). When deciding about the contents of new drug labels and changes in labels for approved drugs, FDA is once again faced with the possibility of both Type I and Type II errors, *i.e.*, providing

inadequate warnings or requiring warning language and contraindications that overstate risk and discourage beneficial use. And once again, the incentives facing FDA in making that decision cause FDA to err on the side of being overly cautious. In deciding not to require a specific warning, for example, the FDA staff faces the prospect of vigorous, public criticism if patients are harmed by the drug, even if the more aggressive warning was not scientifically warranted or would have lead to disincentives in drug usage that outweighed any potential reduction in risks. Far less criticism is likely to occur if the label warns too strongly about harms that in fact almost never occur, or if the label contraindicates certain uses that are likely to be more beneficial than harmful for patients. Patients would probably not know that they had foregone treatments that in fact would have been worth the true risks, and the victims of this FDA error accordingly will never call FDA to task. On the whole, the agency is likely to be far more risk averse than is justified by the actual balance of risks and benefits as known at the time.[4]

[4] For example, the label for Rotateq, the rotavirus vaccine, was recently amended to include a warning against intestinal blockage, a rare but genuine problem with an *earlier* rotavirus vaccine that was removed from the market. FDA took this action even though extremely large clinical trials involving tens of thousands of subjects had revealed no excess likelihood of blockage for Rotateq compared to a placebo. *Label on Merck Vaccine to Disclose a Death*, Wall St. J., May 2, 2008, at B8.

C. State Tort Product Liability Lawsuits Exacerbate the Problems of FDA's Excess Caution.

While advocates of state tort law prescription drug litigation often argue that litigation requirements complement FDA requirements by countering the risk of FDA underwarning or underregulation, the economic analysis of FDA incentives in the drug and drug labeling approval process demonstrates that FDA is far more likely to err in the other direction. Accordingly, rather than creating requirements that cure FDA Type I errors, state tort law creates requirements that exacerbate FDA Type II errors by causing pharmaceutical manufacturers to hold back on seeking approval of new drugs or to add defensive labeling, including further undue contra-indications or overwarnings that further squeeze out physician understanding of more significant labeled information.

In state tort lawsuits, juries necessarily focus on a highly specific personal tragedy rather than on societal trade-offs, giving more weight to the harm allegedly suffered by the plaintiff than to the benefits realized by past and future non-injured users of the drug, because benefited patients will play no role in the trial. Given the one-sided nature of their inquiry, there is little reason to expect the lay jurors' labeling decisions to be superior to those of FDA in terms of balancing the risks and benefits of additional contraindications and warnings on the drug label. *See Riegel v. Medtronic, Inc.*, 128 S. Ct. 999, 1008 (2008). Rather, the jury balance will be skewed in favor of more warnings. Of course, juries will not always decide for the plaintiff. But when they do, there is an excellent chance that the verdict will fault

the manufacturer for failing to provide an over-warning or unwarranted contraindication or warning language that would have unduly cluttered the drug label, given that the label already reflects FDA's excess caution.

The impact of this added layer of tort liability overdeterrence leads to numerous adverse consequences that are contrary to public wellbeing, such as:

1. *Limiting drug availability*: Because prescription drug product liability lawsuits often involve allegations of substantial harm, plaintiff verdicts not uncommonly involve sizable awards for pain and suffering damages, punitive damages, or both. Experience has shown that pharmaceutical firms often treat a large damages verdict as a predictor of more such verdicts to come. *See* Paul H. Rubin, John E. Calfee, and Mark F. Grady *BMW vs Gore*: *Mitigating the Punitive Economics of Punitive Damages*, Sup. Ct. Econ. Rev., vol. 5, pp. 179-216 (1997). While estimates of the cost of liability for pharmaceuticals are few, liability costs are not trivial. For example, a report prepared by the Council of Economic Advisors found that in 2000, liability costs across all U.S. industries were $180 billion, or roughly 1.8 percent of GDP.[5] In the area of drugs and medical devices, Richard Manning identified liability costs for the diphtheria-pertussis-tetanus vaccine by comparing changes in the price of the diphtheria-tetanus vaccine, estimating that at their peak, expected liability costs accounted for roughly 90

[5] Council of Economic Advisors, *Who Pays for Tort Liability Claims? An Economic Analysis of the U.S. Tort Liability System* (2002).

percent of the vaccine's price.[6] In related work, Manning found that differences in product liability regimes can explain much of the difference in Canadian and U.S. prices on drugs.[7]

The expected costs of product liability litigation are added to a firm's cost-benefit analysis in the marketing of drug products and can lead to the unavailability of drug products, both because some patients may no longer be able to afford treatment and because the expected litigation costs may drive products off the market entirely. For example, childhood vaccine manufacturers quickly raised prices and in many cases exited the market in the wake of a few adverse verdicts in the 1980s. *See* Richard L. Manning, *Changing Rules in Tort Law and the Market for Childhood Vaccines*, J.L. & Econ., vol. 37, no. 1, pp. 247-286 (1994). The anti-nausea drug Bendectin was withdrawn from the market in 1983 after a small number of adverse verdicts (which were subsequently reversed), despite FDA insistence that the drug did not cause the birth defects that gave rise to litigation. *See* Paul H. Rubin, John E. Calfee, and Mark F. Grady, *BMW vs Gore*: *Mitigating the Punitive Economics of Punitive Damages*, Sup. Ct. Econ. Rev. vol. 5, pp. 179, 194 (1997); *see also* American Medical Association, Report of the Board of Trustees, *Impact Of Product Liability On The Development Of New Medical Technologies* 1, 79 (1988) ("AMA Board Report") ("Certain older technologies have been removed from the market, not because of sound scientific evidence indicating lack of safety or efficacy

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[6] Richard M. Manning, *Changing Rules in Tort Law and the Market for Childhood Vaccines*, vol. 37, no. 1, J.L. & Econ. 247-75 (1994).

[7] *Id.*

but because product liability suits have exposed manufacturers to unacceptable financial risks.").

2. *Disincentives for Research & Development*: The costs imposed by product liability litigation have an impact not only on the availability of drugs already on the market but on the pipeline for new drugs, because pharmaceutical companies necessarily factor these costs into decisions whether to incur the significant expense required to research and develop drug products and bring them to the market. Where the level of risk is high, the risk of state tort law liability is inversely related to investment in research and development activity.[8] Firms invest less in drugs that promise to provide substantial clinical benefits but also have significant side-effects (such as many drugs for cancer and multiple sclerosis). Thus, particularly to the extent companies are faced with state tort liability risks that are largely divorced from the FDA balancing of risks and benefits in drug and drug labeling approval, the financial payoff from researching these drugs and bringing them to market is reduced, causing fewer such drugs to be made available to patients. *See* Louis Lasagna, *The Chilling Effect of Product Liability Development*, in The Liability Maze: The Impact of Liability Law on Safety and Innovation 334, 335-37 (Peter W. Huber & Robert E. Litan eds., 1991); National Research Council & Institute of Medicine, *Developing New Contraceptives* 141 (1990) (unpredictable nature of litigation is a significant disincentive for fertility research and development); AMA Board Report at 79 ("Innovative new products are not being developed or

[8] Michael J. Moore & W. Kip Viscusi, *Product Liability Entering the Twenty-first Century: The U.S. Perspective* 25, 27 (2001).

are being withheld from the market because of liability concerns.").

3. *Loss of FDA control over drug labeling*: Even a single costly loss in a state tort lawsuit alleging failure to warn imposes a legal standard that effectively requires a manufacturer to make changes in its labeling to avoid anticipated costs of future litigation. Although it theoretically might be possible to change labels only for drugs sold in the state in which the lawsuit was brought (assuming such a state-by-state approach was legal), this seems unlikely. Paul H. Rubin, John E. Calfee, and Mark F. Grady *BMW vs Gore*: *Mitigating the Punitive Economics of Punitive Damages*, Sup. Ct. Econ. Rev., vol. 5, pp. 179-216 (1997). For drugs used in doctors' offices, a state-by-state labeling arrangement would require considerable control over the actions of wholesalers, who are normally free to resell their supply more or less where they please. It would also be hard to prevent patients from using the drug in another state after purchase. Finally, advertising and marketing, which involve risk communication, would become far more complex. Thus it seems likely that the label would be changed nationwide, not just in the state in which the adverse verdict occurred. As a result, a single state tort judgment could effectively wrest control of nationwide drug labeling requirements from FDA, thus depriving the medical community in all states of the benefits of FDA expert determinations on proper and balanced drug warnings.

4. *Defensive labeling*: Firms that suffer adverse verdicts would reasonably attempt to predict other warnings which, if added to the label, might prevent costly litigation in the future. Their competitors, who can be expected to pay close attention to litigation

and its outcomes, would perform similar analyses on their own drugs. With no way to know exactly what would be required through future litigation, firms are likely to add new warning language and contra-indications and create overly crowded labels that seek to anticipate a wide variety of potential plaintiff allegations. *See* Wesley A. Magat and W. Kip Viscusi, *Informational Approaches to Regulation* 1-17, 87-105 (MIT Press 1992) (discussing research showing that substantial increases in the amount of information included on a label decreases the performance of the hazard warning by causing information overload); *see also* W. Kip Viscusi, *Reforming Products Liability* 151 (1991); Aaron D. Twerski et al., *The Use and Abuse of Warnings in Products Liability – Design Defect Litigation Comes of* Age, 61 Cornell L. Rev. 495, 514 (1976). Much of this new warning information would have greater prominence than would be justified by the balance of risks and benefits (precisely because FDA declined to require such information notwithstanding its tendency toward excessive caution). The effect would be to discourage beneficial use of drugs whose labels contain these litigation-induced contraindications and warnings.

As the FDA and others have long recognized, faced with state tort liability regardless of FDA approval of specific warning language, manufacturers may seek to supply warnings about virtually all possible harms that might form the basis for a lawsuit. 71 Fed. Reg. at 3935. For example, a series of Wall Street Journal articles published in 2005 noted that the three erectile dysfunction drugs on the market each carried labels more than 20 pages long. Scott Hensley, *Long Labels Help Drug Firms, But Can Obscure What Matter*, Wall St. J., June 28, 2005; Scott Hensley,

Liability Worries Cloud Drug Labels: In Bloated Package Inserts; Fine Print Can Overshadow Facts of Most Use to Doctors, Wall St. J., July 5, 2005. This litigation-defensive manufacturer tendency to clutter labels with risk information exacerbates FDA's tendency toward excess caution in drug labeling.

5. *Problems exacerbated further in state tort cases alleging missing contraindications*: The concerns discussed above based upon state tort law requirements for added warnings take on particular prominence where, as in this case, a plaintiff is arguing that a drug should have contained a contraindication not required by FDA. Normally, the risk-benefit balancing process for prescription drugs operates at two points: first, when FDA decides what warnings to include on the label and how those warnings are organized, and second, when physicians take account of label warnings as they decide what drugs to prescribe. If failure-to-warn lawsuits cause unfounded or excessive warnings to be placed on the label, physicians can still exercise their usual role in balancing risks and benefits, albeit with less accurate information than would otherwise be available. Contraindications work differently. Physicians are likely to view contraindications as outright bans, because to prescribe in the face of a labeled contraindication is to court a malpractice lawsuit and punitive damages if anything goes wrong. Contraindications therefore largely replace, rather than supplement, the usual balancing of risks and benefits.

Again, there is no reason to expect juries in tort liability trials to perform a better balancing act than FDA. Juries will tend to impose new contraindications, which would prevent physicians from

taking due account of comparative risks and benefits in the highly fact-specific situations in which physicians often making prescribing decisions. As the dynamics of litigation play out, the problem will probably become worse. A contraindication imposed by a jury in one state will likely be translated by pharmaceutical firms into a nationwide contraindication because of the practical inability to limit litigation exposure by single-state label changes. If juries in certain states or regions are especially inclined to find fault with drug labels and impose contraindications, physicians in other states will likely face the same contraindications as label changes are implemented nationwide. Then patients who would have benefited from the contraindicated use will be denied those benefits even if the expected benefit greatly exceeds the likelihood of harm. In extreme cases, manufacturers may choose to remove useful drugs from the market, as happened with many childhood vaccines in the 1980s.

CONCLUSION

The question whether state tort litigation can complement public safety by imposing requirements in excess of those imposed by FDA necessarily depends in part on whether FDA regulation itself is insufficiently or overly cautious. Because FDA is faced with incentives that lead it to stake out overly cautious positions on drug approval and drug labeling, state tort litigation imposing additional requirements leads to a further departure away from the most socially beneficial outcome.

Given this background, it is clear that the public health would only be improved if state tort lawsuits like the one below were held preempted. For the

reasons set forth above, the economist *Amici*, Messrs. Calfee, Berndt, Hahn, Philipson, Rubin, and Viscusi, respectfully submit that the decision of the Supreme Court of Vermont should be reversed.

Respectfully Submitted,

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